

Atty Dkt. No.: 10003511-3  
USSN: 09/628,472

**REMARKS**

In view of the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-15 and Claims 21 to 23, the only claims pending and currently under examination in this application.

Claims 1-9 and 21-22 have been rejected under 35 U.S.C. § 103(a) as being obvious over Dattagupta (A) (4,734,363) in view of Conrad. In making this rejection, the Examiner asserts that because Dattagupta discloses a template dependent polymerase mediated reaction "for producing a mixture of nucleic acid" in which the template is bound to the surface of a bead and Conrad teaches a method in which different plasmids are subjected to reaction conditions that produce a mixture of product nucleic acids from the different plasmids, the claimed invention is obvious.

In response, the Applicants first point out that the term "mixture" is defined in the Webster's online dictionary, available at:

<http://dictionary.reference.com/search?q=mixture>  
as:

- 1) One that consists of diverse elements; or
- 2) A composition of two or more substances that are not chemically combined with each other and are capable of being separated.

As such, the term mixture means a heterogenous composition of two or more distinct substances, e.g., two or more different nucleic acids of differing sequence.

As reviewed in more detail below, Dattagupta describes a method in which a single template is bound to the surface of a bead and then employed in a primer extension reaction to produce a single type of nucleic acid. As such, it is incorrect to characterize Dattagupta as a method of producing a "mixture" of nucleic acids. In fact, since Dattagupta's described utility is to detect a single nucleic acid analyte

Atty Dkt. No.: 10003511-3  
USSN: 09/628,472

using the bead bound template, one would not find any suggestion or teaching in Dattagupta of a method that produces a "mixture" of nucleic acids. Accordingly, to the extent that the Examiner's prima facie case of obviousness is based on this incorrect reading of Dattagupta, the rejection should be withdrawn.

Turning now to the Examiner's prima facie case of obviousness, MPEP § 2142 states that:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, **there must be some suggestion or motivation**, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, **to modify the reference or to combine reference teachings**. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. **The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.** *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). [emphasis added]

It is respectfully submitted that the Examiner's prima facie case of obvious is deficient because:

- 1) the cited references have been impermissably combined using only the Applicants' disclosure as the motivation; and
- 2) even if the teaching of the references are combined, the combined teaching fails to teach or suggest the invention as claimed.

Each of these above summarized deficiencies in the Examiner's prima facie case is now reviewed in greater detail below.

1) Use of impermissible hindsight in combining Dattagupta and Conrad

As summarized above, the MPEP teaches that the Applicants' disclosure cannot be employed for motivation to combine the teaching of two references. Specifically, MPEP § 2143.01 states that:

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the

Atty Dkt. No.: 10003511-3  
USSN: 09/628,472

desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

Furthermore, the MPEP § 2143.01 states that:

A statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levingood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). See also *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000)

As further explained below, the Examiner has combined elements of the prior art in an impermissible manner.

In combining the teachings of the references, the Examiner states that: "It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probe synthesis of Dattagupta et al by immobilizing additional nucleic acids of different sequences for the expected benefit of proving various types of diagnostics based and further based on the broad importance of probe cocktails as taught by Conrad. "

However, as reviewed above, Dattagupta only describes a single type of template immobilized on a given solid support. This is an important feature of Dattagupta's utility in that the structure is a sensitive probe for a single nucleic acid analyte. Dattagupta would not be motivated to modify the beads to each display two or more different templates because then one would not be able to use the structure to detect a single analyte, but just the presence of at least one of two or more different analytes. As such, a motivation to combine the references of Dattagupta and Conrad does not exist in the art as cited, contrary to the assertion of the Examiner.

Accordingly, the only motivation that is present to combine the teaching of Dattagupta and Conrad is the present application. As reviewed above, using an application as motivation for combining references amounts to the use of impermissible hindsight, and is not sufficient to support a combination of references.

Atty Dkt. No.: 10003511-3  
USSN: 09/628,472

Therefore, since the teachings of Dattagupta and Conrad have been impermissably combined, the Examiner's *prima facie* case of obvious is defective and should be withdrawn.

2) Combined Teaching of References Fails to Teach or Suggest all Elements of the Claimed Invention

As reviewed above, even if the teachings of two or more references are properly combined, they must teach or suggest all of the elements of claimed invention in order to render a claimed invention *prima facie* obvious.

In the present case, the claimed invention includes the limitation that one employ:

an array of distinct single-stranded probe nucleic acids of differing sequence immobilized on a substrate

Because the probe nucleic acids of differing sequence must be immobilized on a substrate, i.e., a single substrate, one of skill in the art, in view of the specification, reads the limitation as requiring a structure that is made up of a substrate which includes the distinct nucleic acids immobilized at different and known locations on the surface of the support.

Turning now to the cited references, nowhere in the combined teaching of these references is an array structure as required in the claimed methods taught or suggested. Specifically, the cited combination of references fails to teach or suggest a method that employs a plurality of distinct nucleic acids immobilized on a surface of a **single** solid support.

Accordingly, the combined teachings of the references fail to teach or suggest all of the elements of the claimed invention, i.e., a method that employs a plurality of distinct nucleic acids immobilized on a surface of a **single** solid support.

Atty Dkt. No.: 10003511-3  
USSN: 09/628,472

Therefore, the Examiner's prima facie case of obvious is deficient because:

- 1) the cited references have been impermissably combined using only the Applicants disclosure as the motivation; and
- 2) even if the teaching of the references are combined, the combined teaching fails to teach or suggest the invention as claimed.

As such, Claims 1-9 and 21-22 are not obvious under 35 U.S.C. § 103(a) over Dattagupta (4,734,363) in view of Conrad and this rejection may be withdrawn.

Next, Claims 10-15 have been rejected under 35 U.S.C. § 103(a) as being obvious over Dattagupta (4,734,363) in view of Conrad and further in view of Cantor.

As reviewed above, one would not combine the teaching of Dattagupta and Conrad. Furthermore, one would not combine the teaching of Cantor with at least Conrad because, while Conrad may teach producing a mixture of nucleic acids, Cantor specifically teaches away from producing a mixture of nucleic acids.

Cantor discloses methods in which "master" arrays are used as templates for the production of new duplicate arrays. The disclosed methods in Cantor, including those in which the synthesized nucleic acids are in suspension, require that the distinct synthesized nucleic acids from the template array remain separated from each other. In the preferred embodiments of Cantor, in which duplicate arrays are fabricated from the "master" array, the synthesized nucleic acids must also maintain their spatial integrity with respect to each other such that when they are subsequently immobilized onto a substrate, a functional array is produced. Because Cantor's method is based on keeping synthesized nucleic acids separate from each other, one of skill in the art would have no motivation to combine Cantor with Conrad. As such, this prima facie case of obvious is deficient for this reason.

Furthermore, as demonstrated above, the combined teaching of Dattagupta and Conrad fails to teach or suggest the element of the claimed invention that

Atty Dkt. No.: 10003511-3  
USSN: 09/628,472

requires use of an array of distinct nucleic acids immobilized to a surface of a solid support.

While Cantor may teach an array structure, as pointed out above, Cantor teaches such for use as a master array for the production of replicate arrays, and the method requires that the product nucleic acids be kept separate from each other and employed as probes on the replicate arrays.

Since in combining references it is well established that one must take a reference for all that it teaches, and not just selected portions of a reference, if one were to combine Dattagupta with Conrad and Cantor, one would arrive at a method in which product nucleic acids are kept separate from each other. As such, one would arrive at a method in which the product is not a mixture of nucleic acids, but instead a collection of physically separated distinct nucleic acids.

As reviewed above, an element of the claimed methods is that they produce a mixture of nucleic acids. Since the combined teaching of Dattagupta (4,734,363) in view of Conrad and further in view of Cantor does not teach a method that produces a mixture of nucleic acids, Claims 10 to 15 are not obvious under 35 U.S.C. § 103(a) over these references and this rejection may be withdrawn.

The Applicants also point out that Claim 13 -15 are even further distinguished from the combined teaching of Dattagupta in view of Conrad and Cantor because Claim 13 requires that the product target nucleic acids produced by the method of Claim 10 be contacted with an array of probe nucleic acids. In contrast to this step, Cantor's disclosed method is directed to making nucleic acids that are used as probes and immobilized on a support to produce a replicate array of a master, and as such the product nucleic acids are not contacted with an array of probe nucleic acids.

Finally, Claim 23 has been rejected under 35 U.S.C. § 103(a) as being obvious over Dattagupta (A) (4,734,363) in view of Conrad and further in view of Dattagupta (B) (5,215,899). As reviewed above, the Dattagupta (A) in view of

Atty Dkt. No.: 10003511-3  
USSN: 09/628,472

Conrad represents an impermissible combination of references that, even if combined, fails to teach or suggest the element of the claimed invention that requires use of an array of distinct nucleic acids immobilized to a surface of a solid support. As the Dattagupta (B) reference has been cited solely for the concept of employing a strand displacement amplification protocol, Dattagupta (B) fails to make up the deficiency in the teachings of the primary references. Accordingly, Claim 23 is not obvious under 35 U.S.C. § 103(a) over Dattagupta (A) in view of Conrad and further in view of Dattagupta (B) and this rejection may be withdrawn.

Atty Dkt. No.: 10003511-3  
USSN: 09/628,472

**CONCLUSION**

The applicant respectfully submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Gordon Stewart at 650 485 2386. The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078.

Respectfully submitted,

Date: September 2, 2004

By:

Bret E. Field  
Registration No. 37,620

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**